PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC25670A	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/IB2005/000100	International filing date *(day/month/year)* 17.01.2005	Priority date *(day/month/year)* 30.01.2004
International Patent Classification (IPC) or national classification and IPC INV. A61K47/10		
Applicant PFIZER PRODUCTS INC. et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25.02.2005	14.07.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Epskamp, S Telephone No. +31 70 340-2857

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2005/000100

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-44	as originally filed
Claims, Numbers	
1-9	received on 28.06.2006 with letter of 28.06.2006
Drawings, Sheets	
1/4-4/4	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 9 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. 9 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*.

☐ no international search report has been established for the said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9
Industrial applicability (IA)	Yes:	Claims	1-8
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 9 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:
D6: WO 03/009848 A

Novelty

1 - Claims 1-9 are considered novel (Article 33(2) PCT).

2 - Document D6 (page 11, lines 1-5; example 1) discloses a composition comprising a compound of Formula I, SBE cyclodextrin, and water, but does not disclose the inclusion of a preservative.

Inventive Step

3 - The composition of claim 1 differs from closest prior art D6, in that it includes a preservative. The features of "improved injection site toleration" and "the preservative [demonstrating] pharmaceutically acceptable preservative effectiveness" cannot be seen as distinguishing features, as they are vague and ill-defined and merely amount to stating results to be achieved.

The problem to be solved by claim 1 can thus only be seen as providing a composition with improved preservation.

Claim 1 cannot be considered inventive (Article 33(3) PCT), as the addition of a preservative to the composition disclosed in D6 in order to provide preserved compositions is well within the skilled person's abilities without excercising an inventive step. In this respect claim 1 can only be seen as defining a result to be achieved.

4 - Mutatis mutandis the same arguments apply to independent claims 8 and 9, which are thus also considered to lack an inventive step.

5 - Dependent claims 2-7 do not appear to contain any additional features which, in

combination with the features of any claim to which they refer, involve an inventive step with respect to the prior art named in the present proceedings. The reasons therefor are that the additional features of the said dependent claims are either directly known from document D6, or they concern minor modifications which lie within the normal practice of the skilled person.

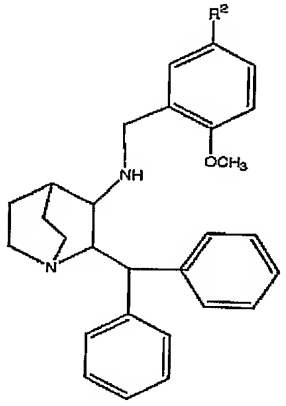
Industrial applicability

6 - Claims 1-8 fulfill the requirements of Article 33(4) PCT (see also Item III).

PC25670/PCT Amended claims June 2006

CLAIMS

1. A pharmaceutical composition with an improved injection site toleration comprising a therapeutically effective amount of an Active Pharmaceutical Ingredient, a β-cyclodextrin, a pharmaceutically acceptable preservative, a pharmaceutically acceptable vehicle, and an optional pharmaceutically acceptable excipient, wherein the preservative demonstrates pharmaceutically acceptable antimicrobial preservative effectiveness and wherein the Active Pharmaceutical Ingredient is a compound of Formula I,



I

or its pharmaceutically acceptable salts, wherein R^2 is selected from the group consisting of methyl, ethyl, isopropyl, *sec*-butyl and *tert*-butyl.

2. The pharmaceutical composition according to Claim 1 wherein the β-cyclodextrin is 2-hydroxypropyl- β-cyclodextrin or sulfobutyl ether-β-cyclodextrin.

3. The pharmaceutical composition according to any preceding claim wherein the preservative is selected from thimerosal, propylene glycol, phenol, or meta-cresol or a combination thereof.

PC25670/PCT Amended claims June 2006

4. The pharmaceutical composition according to any preceding claim wherein the preservative has a binding value to the cyclodextrin that is less than a binding value of the Active Pharmaceutical Ingredient to cyclodextrin.

5. The pharmaceutical composition according to any preceding claim wherein about 1 mg/mL to about 5 mg/mL of the preservative is unsequestered in the cyclodextrin.

6. The pharmaceutical composition according to any preceding claim wherein the binding value of the Active Pharmaceutical Ingredient to cyclodextrin is between 500 M^{-1} and 10,000 M^{-1}.

7. The pharmaceutical composition according to any preceding claim for use as a medicament.

8. The use of a composition according to any of Claims 2 to 6 in the manufacture of a medicament for the treatment of a disease for which a neurokinin receptor antagonist is indicated.

9. A method for the treatment of a disease for which a neurokinin receptor antagonist is indicated in mammals comprising administering to said mammal a therapeutically effective amount of a pharmaceutical composition of any of Claims 2 to 6.